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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
07/21/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,014	PAN ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 6, 8, 16 and 45-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,8,16,45 and 46* is/are rejected.

7)☒ Claim(s) *10 and 47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed 4/29/10 is acknowledged. Claims 2-5, 7, 9, 11-15, 17-44 are cancelled. Claims 1, 6, 8 and 16 are amended. Claims 45-47 are newly added (it is noted that two "claim 45" were newly added and submitted on 4/29/10. The duplicate claim 45 and claim 46 have been renumbered as claims 46 and 47). Claims 1, 6, 8, 16 and 45-47 are pending in this application and under examination with respect to SEQ ID NOs: 1, 3 and 36 in this office action.

2. Applicant's arguments filed on 4/29/10 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

3. The rejection of claims 1, 6, 8 and 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 4/29/10, the following rejections are maintained.

Claim Objections

4. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When

claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 45 (duplicate claim #45) and 46 have been renumbered as claims 46 and 47.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 8, 16 and 45-46 (original duplicate claim 45) are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a purified polypeptide BNP2 comprising the amino acid sequence of SEQ ID NO: 3 and 36, does not reasonably provide enablement for a structurally and functionally undefined polypeptide comprising an amino acid sequence having at least 91% to 97% identity to the amino acid sequence of SEQ ID NO:1 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in the scope with these claims. The rejection is maintained for the reasons made of record and the reasons set forth below.

Claims 1, 6, 8, 16 and 45-46 (original duplicate claim 45) as amended are directed to a purified mature BNP2 polypeptide comprising an amino acid sequence

having at least 91% or 97% identity to the amino acid sequence of SEQ ID NO:1 and a pharmaceutical composition comprising the claimed polypeptides.

On p.5-6 of the response, Applicant argues that instant claims are fully enabled because the amino acid sequence of SEQ ID NO:1 is a 33-amino acid polypeptide present at the C-terminus of human BNP2. Applicant further argues that the RNA encoding the polypeptide of SEQ ID NO:1 and the protein can be detected in heart tissue from heart failure patients in examples 1 and 5. Applicant argues that the specification also teaches a variety of other species having 91% or 97% identity to SEQ ID NO:1 at paragraph [0030] and thus a skilled artisan would know how to make and use the claimed polypeptides without undue experimentation. Applicant's arguments have been fully considered but they are persuasive.

In contrast to Applicant's arguments, the specification only discloses that an up-regulated expression level of SEQ ID NO:3 and 36 is found in heart tissue from heart failure patients. The specification fails to provide sufficient guidance as to how all the polypeptides comprising fragments and variants with at least 91% or 97% identity to the amino acid sequence of SEQ ID NO:1 as in instant claims are related to the amino acid sequence of SEQ ID NO:3 or 36. The specification does not show that the claimed variant polypeptides comprising an amino acid sequence having at least 91% or 97% identity to the amino acid sequence of SEQ ID NO:1 are also up-regulated and thus would be associated to the same disease or other diseases as in SEQ ID NO:3 or 36.

The specification also fails to show that whether the claimed variant polypeptides comprising an amino acid sequence having at least 91% or 97 identity to SEQ ID NO:1 would act in the same manner as SEQ ID NO:3 and 36 in the patients suffering from heart failure and thus can have the same utility as SEQ ID NO:3 and 36.

As previously made of record, the events of transcription and translation of each gene are independent from each other. The specification fails to show that the transcription and translation of the claimed polypeptides and variants comprising an amino acid sequence at least 91% or 97% identity to SEQ ID NO:1 are positively associated with SEQ ID NO:3 and 36 and thus can also be used as an diagnostic marker of heart failure. Thus, it is unpredictable whether all the claimed variant polypeptides comprising an amino acid sequence having at least 91%-97 identity to SEQ ID NO:1 are useful for a diagnostic marker of any diseases or other purposes since there is no guidance to indicate how the variant polypeptides are related to SEQ ID NO:3 or 36. It is also unpredictable which, if any other variant polypeptides would be similarly upregulated, since the regulation of a gene or a protein is not dependent on the sequence of the protein. Since the specification fails to provide sufficient guidance as to whether the variant polypeptides would be up-regulated and whether they are related to heart diseases or other diseases, a skilled artisan cannot contemplate how to use the claimed variant polypeptides. Thus, a skilled artisan cannot contemplate how to use the claimed genus of variant polypeptides except SEQ ID NO:3 and 36.

Note that the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such

guidance, it is unpredictable what changes can be made and still maintain activity; it is also unpredictable whether the claimed undefined polypeptide variants can have the same utility as SEQ ID NO:3 or 36 as a diagnostic marker; and thus the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03.

Accordingly, the rejection of claims 1, 6, 8, 16 and 45-46 (original duplicate claim 45) under 35 U.S.C. 112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is maintained.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 4/29/10.

Claim Rejections - 35 USC § 112

6. Claims 1, 6, 16 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims as amended are directed to a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1 and a pharmaceutical composition comprising the claimed mature BNP2 polypeptide. The instant claims now recite a new limitation "an amino acid sequence having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1", which was not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such new limitation recited in the present claims, which did not appear in the specification or original claims, as filed, introduces new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The specification fails to disclose the new limitation "an amino acid sequence having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1" as recited in claims 1, 6, 16 and 45. The specification only discloses "at least about 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or more percent identity over that length to the amino acid sequence set forth in SEQ ID NO:I or 2" on p. 8 of the specification. In addition, the specification only teaches a single data point; eg. the C-terminal BNP2 sequences from human (SEQ ID NO: 1) and orangutan (SEQ ID NO:7) having about 91% identity and the C-terminal BNP2 sequences from human (SEQ ID NO:l), chimpanzee (SEQ ID NO:9), and gorilla (SEQ ID NO:12) having about 97% identity on p. 9 of the specification. What is disclosed is one or two examples of proteins that have

a given percent identity to a given sequence. This is a species disclosure. But the claims are directed to a genus of polypeptides having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1 (any protein with 3-9% variation from a given sequence). However, the specification fails to teach such genus of polypeptides having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1. Accordingly, in the absence of sufficient recitation of the new limitation, the specification does not provide adequate written description to support "an amino acid sequence having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1" as recited in claim 1. Support is not found for such new limitation as disclosed in the original specification and thus the recitation constitutes new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitation.

Conclusion

Allowable Subject Matter

7. Claims 10 and 47 (original newly-added claim 46) are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

On p. 7 of the response, Applicant argues that in light of the amendment and the remark, the objection to claim 10 is moot. In contrast to Applicant's arguments, claim 10 is still objected to because claim 1 is still rejected (see the rejection set forth above).

8. Claims 1, 6, 8, 16 and 45-46 (original duplicate claim 45) are rejected.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang
June 30, 2010

/Christine J Saoud/
Primary Examiner, Art Unit 1647